REMARKS

Claims 1, 4 – 8, and 10 are pending. Claims 1 and 10 have been amended. Support for these amendments may be found in the Specification at, for example, page 2, lines 20 – 22, and Examples 2 - 6, pages 4 - 6.

Claims 1, 4 – 8, and 10 are finally rejected under 35 U.S.C. §103(a) as being unpatentable over Lanier et al. (Clinical Therapeutics, July 2002) in view of Kim (US 5,976,573) and further in view of Ray et al. (Journal of Allergy and Clinical Immunology, 1999) and Castillo et al. (US 6,743,439). According to the Examiner, Lanier et al teach the efficacy of combined fluticasone (nasal) and olopatadine (ophthalmic) in the treatment of allergic rhinoconjunctivitis (allergic rhinitis combined with allergic conjunctivitis). The Examiner also notes that Lanier et al. teach the effective amount of olopatadine (0.1%) for the treatment of rhinoconjunctivitis. The Examiner does acknowledge that Lanier et al. do not teach olopatadine and fluticasone "in a single, nasal aqueous composition, specified particle size of fluticasone, pH and viscosity." The Examiner cites Castillo et al. for what the Examiner asserts is a teaching that olopatadine compositions can be administered nasally. The Examiner concludes that it would have been obvious to combine the teachings of the four cited references and arrive at a topically administrable nasal composition comprising olopatadine and a steroid as recited in Applicants' claims.

In response, Applicants respectfully traverse the §103(a) rejection to the extent it may apply to the amended claims. As amended, Applicants' claims recite a method of treating allergic rhinitis comprising <u>intranasally</u> administering a composition comprising <u>at least 0.4% (w/v) olopatadine</u> and a specified amount of a steroid selected from the list recited in Applicants' Claim 1. Lanier et al. concluded that the combined use of a nasal spray with a topical eye drop was more effective in the treatment of rhinoconjunctivitis (which includes symptoms of the nose and the eyes) than the combined use of a nasal spray with a systemic tablet. Lanier et al. does not disclose or suggest incorporating olopatadine into an intranasal composition, and certainly does not disclose or suggest incorporating olopatadine into an intranasal product for alleviating <u>nasal</u> symptoms.

The Examiner then cites Castillo et al. for a teaching that ophthalmic compositions of olopatadine are administrable nasally. The Examiner is impermissibly using hindsight to

extract this teaching from Castillo et al. A fair reading of the Castillo et al. reference by one skilled in the art does not necessarily lead to that conclusion. The Castillo et al. reference teaches a new solution vehicle that can is particularly well suited for topical ophthalmic use but can also be used for otic or nasal administration. The vehicle is described as an aqueous vehicle that contains a cationic preservative, a cationic drug, and a sulfonated styrene/maleic anhydride copolymer. These solution vehicles are superior to prior art vehicles that contained polystyrene sulfonic acid polymers because those polymers interact with the cationic preservative and reduce the preservative's efficacy. The Castillo et al. patent is based, among other factors, on the finding that solution compositions comprising a sulfonated styrene/maleic anhydride copolymer are easier to preserve than similar compositions comprising polystyrene sulfonic acid. See Castillo et al. at Col. 2, lines 1 – 5, and Examples 3, 4, and 5 at Col. 5, line 1 – Col. 7, line 16. As for the cationic drugs that are suitable for use in the solution vehicles of the Castillo et al. invention, olopatadine is but one of a list of preferred drugs. The reference teaches that any pharmaceutically acceptable drug compound may be used. The preferred drugs have both a ring structure and an amine functional group. See Castillo et al. at Col. 2, lines 11 – 24. One skilled in the art would not take from these excerpts from the Castillo et al. reference a conclusion that the Castillo et al. reference teaches that olopatadine compositions can be administered intranasally and be pharmaceutically effective. Instead, one skilled in the art would conclude from the Castillo et al. reference that the vehicles of Castillo et al. could be used for ophthalmic, otic or nasal drugs that were otherwise intended to be topically administered. That is, the Castillo et al. reference simply teaches that the vehicle is suitable for nasal administration, not that any particular olopatadine compositions are suitable for nasal administration.

Even assuming for the sake of argument that Castillo did suggest the topical nasal use of olopatadine, the forced combination of cited references proposed by the Examiner does not yield Applicants' claimed method. There is no suggestion or disclosure of the use of olopatadine in an amount of at least 0.4% in combination with a steroid in any of the cited references, taken alone or in combination.

Moreover, as noted in Applicants' Amendment dated April 22, 2005, the selection of olopatadine as an anti-allergy agent to be combined with a steroid in an intranasal composition provides a special safety feature that conventional anti-histamine agents do not. This safety advantage is neither disclosed nor suggested by any of the references cited by the Examiner.

Applicants direct the Examiner's attention to the attached article: Brockman et al., "Interactions of olopatadine and selected antihistamines with model and natural membranes," Ocular Immunology and Inflammation, 11(4):247-268 (2003), which is co-authored by one of the inventors of the present application. This article demonstrates the different effects or consequences that olopatadine and antihistamine agents have on interactions with cell membranes. The article concludes that olopatadine is unique because it does not cause non-specific interactions with cell membranes that can lead to cell damage. Thus, unlike conventional antihistamine agents, olopatadine is unlikely to cause histamine release or non-specific cell membrane damage and the 'rebound effect' that antihistamine nasal sprays commonly have where extended use leads to exaggerated nasal symptoms.

Applicant believes that the above amendments and remarks have placed Claims 1, 4 – 8, and 10 in condition for allowance. Accordingly, allowance of the claim in this application is respectfully requested.

Respectfully submitted,

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1/13/06
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